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Comparison of End-Tidal Breath CO (Carbon Monoxide) Estimates of COHb with Estimates Based on Exposure Profiles of Individuals in the Denver and Washington, DC Area

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COMPARISON OF END-TIDAL BREATH CO ESTIMATES OF COHb WITH ESTIMATES BASED ON EXPOSURE PROFILES OF INDIVIDUALS IN THE DENVER AND WASHINGTON, DC AREA

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Abstract

The U.S. Environmental Protection Agency has sponsored a field study of personal exposures to carbon monoxide (CO) in Washington, DC and Denver. CO concentrations in exhaled breath were measured in 837 nonsmoking adult residents of Washington and 454 nonsmoking adult residents of Denver between November 18, 1982 and February 28, 1983. The percent of people exceeding 10 ppm (about 2% COHb saturation) was 10% in Denver and 5% in Washington. Mean (± S.E.) breath concentrations were 7.2 ±0.2 ppm in Denver and 5.1 ±0.2 ppm in Washington. These concentrations agreed well with a previous nationwide study of blood carboxyhemoglobin (NHANES II), but were higher than would be predicted from outdoor fixed stations. Comparisons of COHb estimated from breath measurements and COHb estimated by CO exposures and the Coburn-Forster-Kane (CFK) equation indicate a discrepancy, with the breath COHb tending towards higher estimates. Possible contributing factors to the discrepancy are uncertainties in published breath CO-blood COHb correlations, a tendency for the personal monitors to drift with time, and uncertainties in physiological function values used in the CFK equation.

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INTRODUCTION

Two field studies to monitor personal exposures to CO were performed in Washington, DC, and Denver, Colorado, during the Winter of 1982-1983. These studies were conducted to demonstrate a methodology for measuring the distribution of personal exposures to air pollution in the general public.

This paper, 121.5, is the fifth paper in a series of presentations that describe the design and conduct of these two studies. Paper 121.1 gives the background concepts, purpose and overview of these studies.[1] Paper 121.2 describes the personal exposure monitor (PEM) used in the conduct of these studies.[2] Paper 121.3 presents the details of the survey in Denver and the results of the CO exposure data collections in Denver.[3] Paper 121.4 describes the details of the survey in Washington, DC, and the results of the CO data collections in Washington, DC.[4]

The reader is referred to these four previous papers for more detailed information on these studies which led to the collection of the CO data sets discussed in this paper.

Study Design

Participants in Washington, DC, and Denver were nonsmokers selected by a stratified probability sampling scheme to represent the non-instutionalized metropolitan area populations over 17 years of age. In Denver, each person carried a monitor for 48 hours and gave a breath sample in the evening of each day. In Washington, each participant carried a monitor for only 24 hours and gave a single breath sample that evening. Participants kept a record of their activities, including commuting, cooking with gas stoves, and other CO-related activities.

Description of Methods

Breath. A total of 870 breath samples (including 58 duplicates) were collected from 812 participants in Washington. In Denver, 895 breath samples were collected from 454 participants. Breath samples were collected in the subjects' homes using 1-L bags (Energetics Science Division, Becton-Dickinson). Breath sampling was by the standard method of Jones.[5] The subject takes a deep breath, expels the vital capacity air from his lungs, takes a second deep breath, holds it for 20 seconds to allow the alveolar CO to approach equilibrium, expels the first part of his vital capacity breath into the room to remove the dead space air and the end-tidal part into the bag. The bags were clamped and transported to a central laboratory. The breath CO was analyzed the same evening, by attaching the bag to a manifold equipped with an activated charcoal/Purafil filter to remove hydrocarbon interferences. In both locations, all breath samples were analyzed using a single General Electric CO-3 electrochemical detector. The detector was calibrated before, during (Washington only), and after each set of daily breath samples. Multipoint calibrations were also performed routinely. In Washington, a strip chart recording was made and the value read to the nearest 0.1 ppm after the trace stabilized (generally within five minutes). In Denver, the readings were made directly from the instrument's readout display; thus readings were made only to the nearest part per million. The procedural differences arose due to two different contractors performing the studies.

Air. Personal exposures to CO were measured with a portable battery-powered instrument (the CO-ED I) consisting of a modified GE CO 3 detector and a MAGUS DL-1 data logger. Outdoor concentrations were measured at 15 locations in Denver and 11 in Washington, DC, using EPA-approved instruments employing non-dispersive infrared (NDIR) methods. Daily calibrations were performed on the CO-ED and NDIR instruments. Periodic audits were performed during the course of the study by technicians from EPA's Environmental Monitoring Systems Laboratory (EMSL-RTP) in Research Triangle Park, NC.

Quality Assurance

Several experiments were carried out to determine instrument noise, response time, permeability of the sample bags to CO, effect of storage time, precision, and interferences. Instrument noise was on the order of ±0.2 ppm. Response time (to 95% of the final reading) was less than 2.5 minutes for all CO concentrations tested (up to 50 ppm). Two types of bags were tested for CO recoveries: 600 ml blood transfer bags (Fenwal, Inc.) and the 1-L Energetics Science (ESD) bags. The Fenwal bags showed an average loss of 1.7 ±0.5 ppm CO while ESD bags lost only 0.3 ±0.2 ppm CO over the maximal time span between collection and analysis of 24 hours. The losses were independent of the CO concentrations introduced into the bags (2.5 - 15 ppm in both dry air and 75% relative humidity).

Contamination of the ESD bags during storage was tested by filling them with humidified zero air and storing them for 0 - 20 hours at 50 ppm CO. The CO concentration was unaffected. Air spiked with ethanol, acetaldehyde, and propionaldehyde did not affect the CO readings when passed through the activated charcoal filter, but caused immediate large instrumental responses when the filter was removed.

Precision of the breath sampling was tested on eight non-smokers who gave four breath samples each. Differences in readings ranged between 0 and 0.1 ppm for seven of the eight subjects, with corresponding coefficients of variation (CV) of 0-5%. The range for the eighth subject was 0.4 ppm (CV = 16%).

Quality control activities during the Washington study included sending breath bags filled with different CO concentrations (0, 3.5, 10, and 40 ppm) to the field and analyzing them concurrently with the field samples. Duplicate breath samples were collected from 7% of the participants. Quality control data for blanks, controls, and duplicates in Washington were also collected. Blank values (N = 147) never exceeded 0.2 ppm and averaged 0.05 ppm. Breath bags spiked at three concentrations (N = 140) showed 99% recoveries for two of them and 95% for the third. Relative standard deviations for the 140 control samples averaged less than 2%. Duplicates (N = 58) showed mean differences of 0.11 ppm, over a range of 2-20 ppm.

Quality assurance audits of the breath sampling system were run by EMSL-RTP technicians in November 1982 and February 1983. In Denver and Washington, both audits showed the systems were performing well within the ±10% targets, with a tendency to read 5-10% low at the lowest (5 ppm) concentrations.

COMPARISON OF OBSERVED END-TIDAL BREATH CO WITH PREDICTED COHb

It is possible to estimate each individual's blood COHb (%) from the breath data by using the following formula,[5,6] where BCO denotes the breath CO concentration in parts-per-million (ppm):

$$COHb = 0.2\ BCO/(1 + 0.002\ BCO)$$

Because the coefficient of BCO inside the parentheses is quite small, it is possible to approximate this equation as COHb = 0.2 BCO, or BCO = 5 COHb. Although experimental work in this area is somewhat limited, most existing investigations support this relationship between end-tidal breath CO and blood COHb quite closely.[5-10]

The CO personal exposure monitor (PEM) data logger sampled the CO concentration profile continuously and computed the average CO concentration automatically. Each time the respondent changed his activity, he pressed a data logging button on the PEM which automatically stored the exact time and the average CO concentration since the previous button-pressing. Thus, the resulting average CO concentrations throughout the day are available on each respondent. For each person, these CO readings and times were entered into the Coburn-Forster-Kane CO-COHb equation.[11] Because physiological information on each person was not available, two different sets of "typical" physiological characteristics were chosen for men and women (see Appendix A). The alveolar ventilation rate (VA) for each person was assumed to vary as a function of the subject's physical activities throughout the day (sleep, sedentary activity, light work, and heavy work). These activity levels were keyed to the activities recorded by respondents on their diaries. Using this information, it was possible to compute the estimated COHb as a function of time for each respondent from their CO exposure profile as a function of time. The initial conditions at the beginning of each 24-hour period were estimated by running the model for the previous 24-hour period using exactly the same CO exposure profile of the person.

By the above approach, it was possible to compute the predicted blood COHb level at the time that the breath sample was taken (breath samples were taken when the PEM was picked up) and to compare the result with the breath sample using the above equation.

How should these comparisons be made? A number of statistical approaches were examined for this purpose. These approaches can be illustrated using the data from Washington, DC.

Distribution of Paired Differences. One direct approach is to compute the difference Di between observed breath CO concentrations Xo and the predicted breath CO concentration Xp:

$$Di = (Xo - Xp)i$$

This result is the random variable Di which can be expressed graphically on a histogram.

To plot the findings for Washington, DC, the difference between the observed breath reading BCO and COHb predicted by the CFK model (and converted to an equivalent breath reading in ppm) was computed for each respondent i:

$$Di = (BCO - 5[COHb])i$$

The resulting histogram of 625 values of Di in Washington, DC, has a long tail to the right (Figure 1), with values ranging as high as 40 ppm. If a cutoff is established above D = 10 ppm, then the right-skewness is less pronounced and the remaining data are more symmetrical. A total of 10 respondents lie above the 10 ppm cutoff, and there is reason to believe that their high breath readings may be due to undeclared smoking activities on their part. Without these 10 anomalous values, D ranges from -8 ppm to +10 ppm, with an approximate center at +2 ppm, and it has the appearance of a normal distribution.

Standard Regression; Model Predicted COHb vs. Observed Breath COHb. When comparing two sets of paired observations, it is common practice to plot the two variables on cartesian coordinates and to apply the technique of standard linear regression analysis. We typically plot the independent variable on the (horizontal) X-axis and the dependent variable on the (vertical) Y-axis. The standard linear regression technique provides the slope and vertical intercept of the unique straight line which minimizes the sum of the squares of the vertical distances between the data points and the resulting line.

To apply the standard regression approach, the observed breath readings (BCO) for 625 respondents in Washington, DC. were treated as the independent variable and were plotted on the horizontal axis, and the blood COHb levels (converted to breath levels in ppm) predicted by the CFK from the CO exposure profiles of each person were plotted on the vertical axis (Figure 2). The resulting linear regression line had a slope of 0.322, with R-squared = 0.342, suggesting that this linear model explained 34% of the variability.

Because the analysis of paired differences described above led us to suspect that 10 persons out of the total sample of 625 were "secret smokers" that were erroneously included in our sample, the regression approach was repeated with these 10 persons excluded (Figure 3). The resulting linear regression line had a slope of 0.564, with R-squared = 0.567, suggesting that the linear model now explained about 57% of the variability.

In such an analysis, if no error were present and if the model were completely accurate, then all data points would lie exactly on the 45-degree line, Xp = Xo. If there is systematic error in the predicted value, then one would expect to find vertical scatter equally both above and below the 45-degree line. Because more data points lie below than above the 45-degree line, and because the slope of the line is less than 1.0, both figures suggest that observed readings are higher than predicted readings.

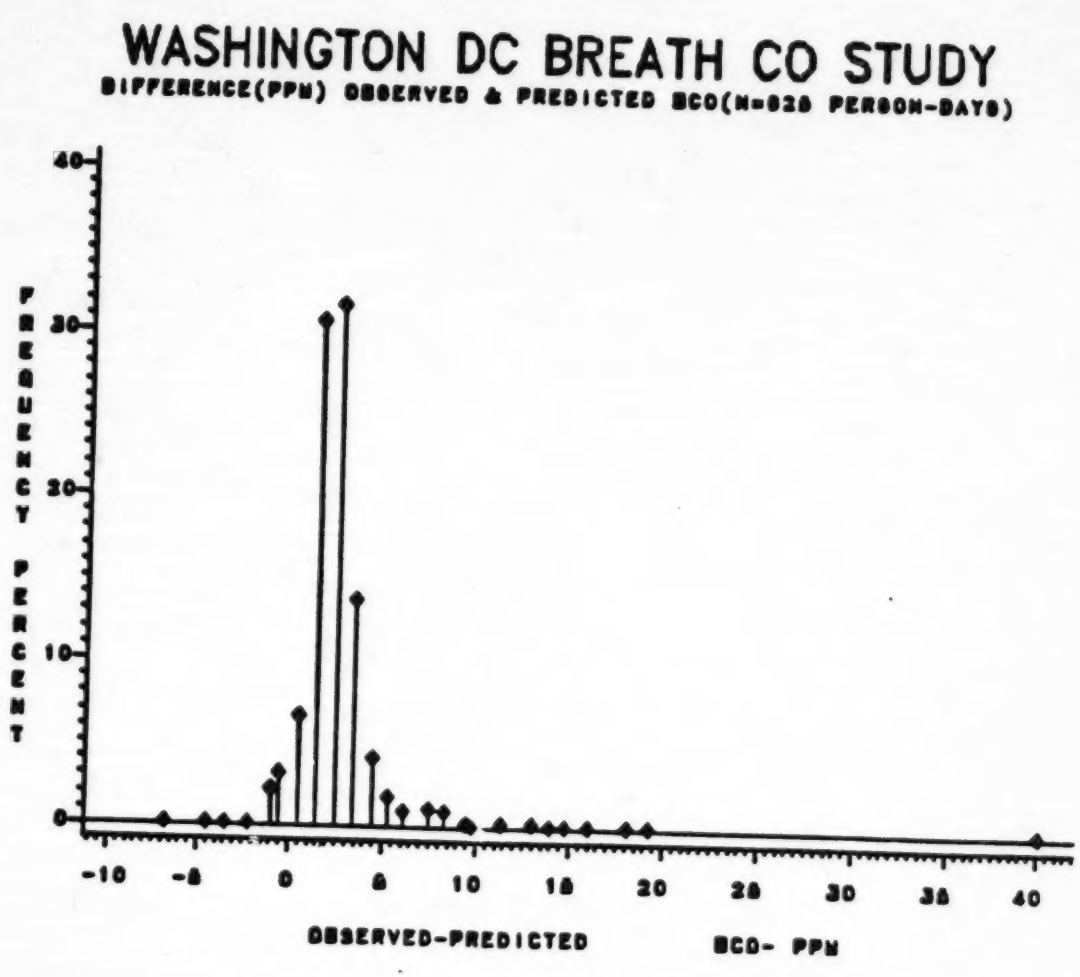

FIGURE 1. HISTOGRAM OF DIFFERENCES (D_i) BETWEEN OBSERVED BREATH CO (X_o) AND PREDICTED BREATH CO (X_p) IN WASHINGTON, D.C., WHERE $D_i = (X_o - X_p)_i$ TEN VALUES OF $D_i > 10$ ppm MAY BE DUE TO CIGARETTE SMOKING.

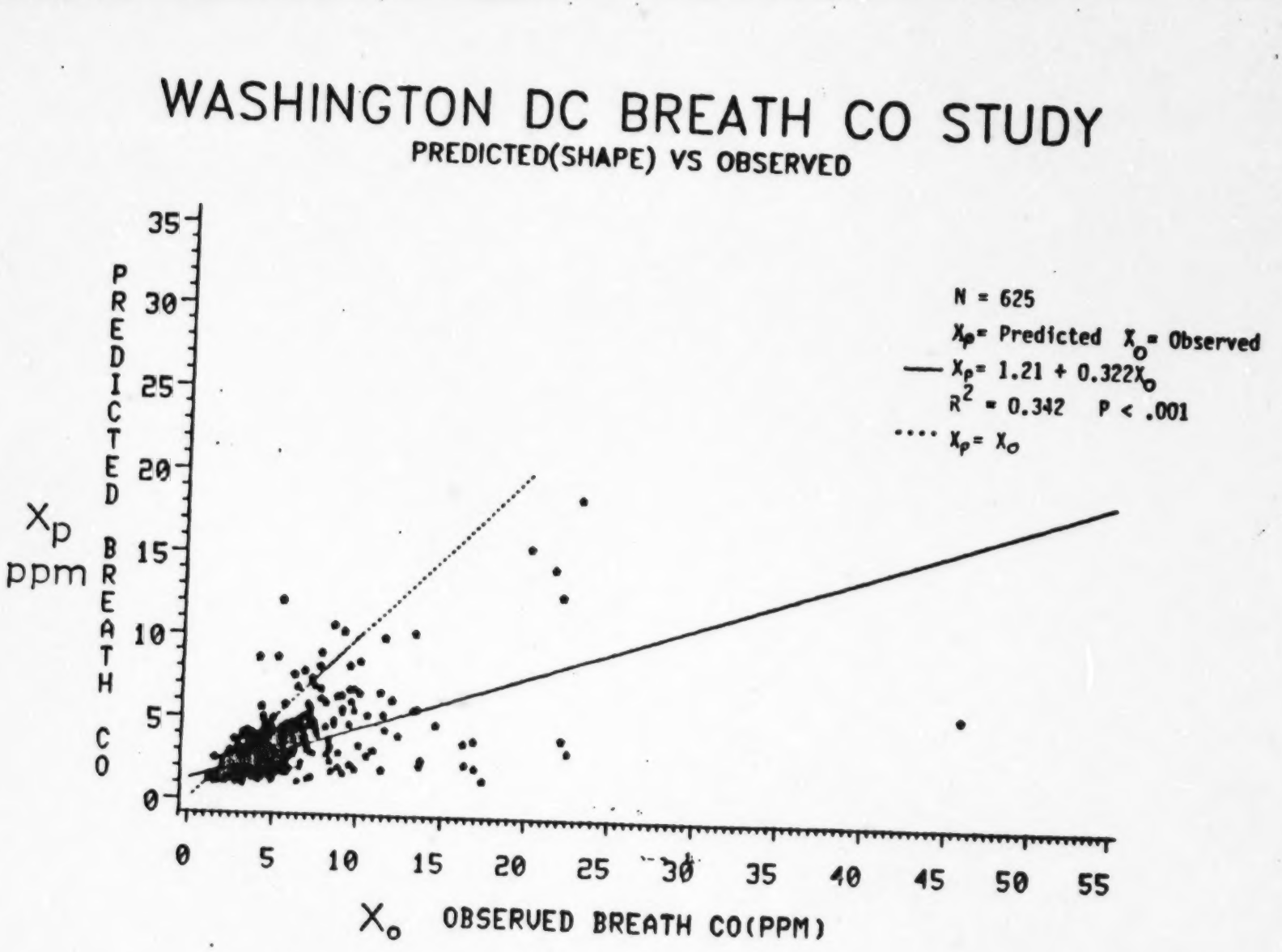
WASHINGTON DC BREATH CO STUDY
PREDICTED(SHAPE) VS OBSERVED
N = 625
X_p= Predicted X_o= Observed
$X_p = 1.21 + 0.322X_o$
$R^2 = 0.342$ P < .001
$X_p = X_o$
X_p ppm
PREDICTED BREATH CO
0 5 10 15 20 25 30 35
0 5 10 15 20 25 30 35 40 45 50 55
X_o OBSERVED BREATH CO(PPM)

FIGURE 2. PREDICTED BREATH CO CONCENTRATION (X_p) VERSUS OBSERVED BREATH CO CONCENTRATION (X_o) IN WASHINGTON, D.C.: N=625 PERSON-DAYS.

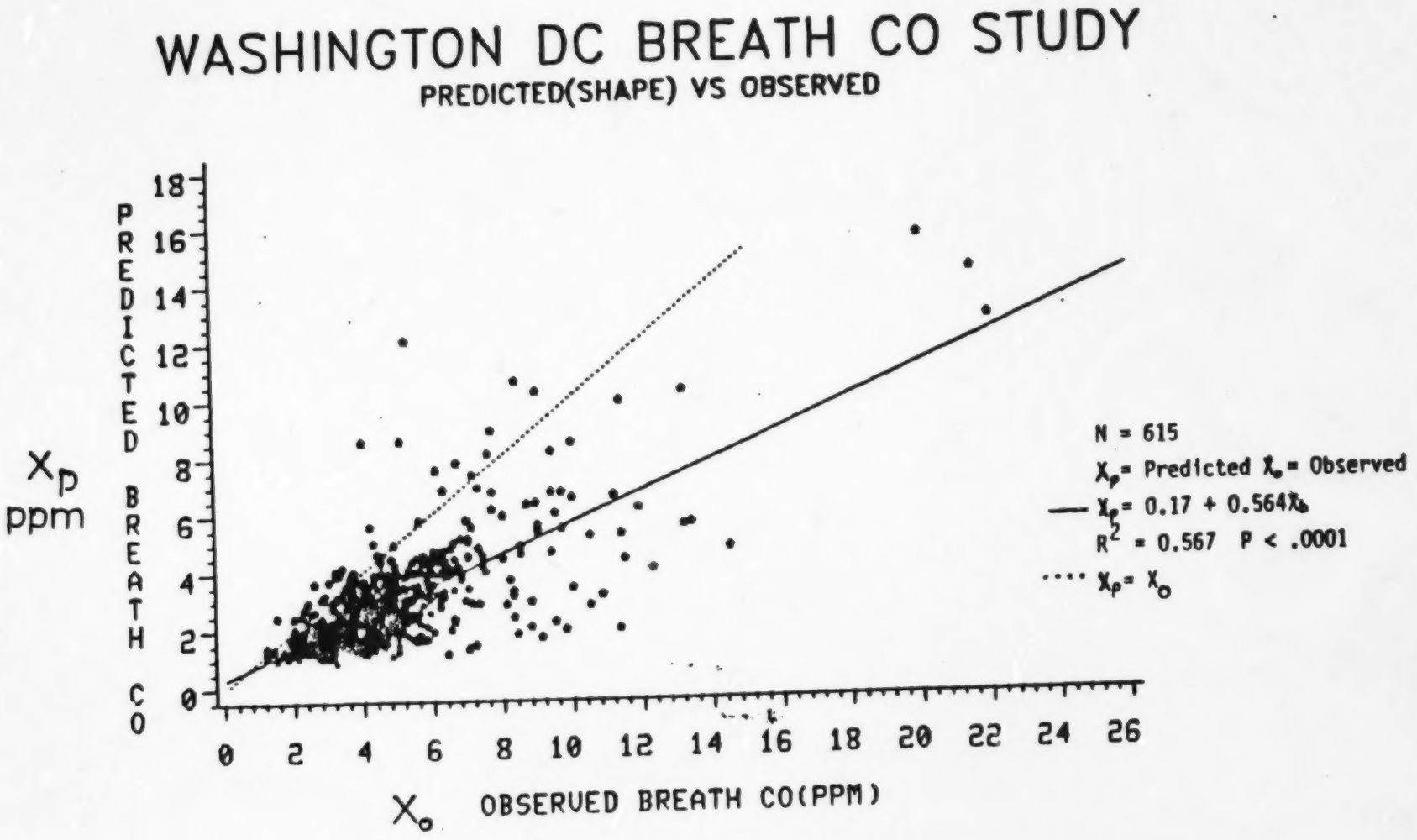

FIGURE 3. PREDICTED BREATH CO CONCENTRATION (X_p) VERSUS OBSERVED BREATH CO (X_o) IN WASHINGTON, D.C.: EXCLUDING 10 OUTLIERS N=615 PERSON-DAYS.

Standard Regression; Observed Breath COHb vs. Model Predicted COHb. Suppose that a perfect model were available and that its predictions were known to be completely accurate. Then it would be reasonable to assume that all the error present was in the observed variable, with no error in the predicted variable. However, linear regression finds the line which minimizes the sum of the squares of the distance (and hence the error) only in the vertical direction, which happens to be the axis on which the predicted variable is plotted. Thus, it would make sense, if such a perfect model were available, to reverse the axes, plotting the predicted variable (COHb) on the horizontal axis and the observed variable (BCO) on the vertical axis. In the case of the Denver-Washington, DC, field studies, a sensitivity analysis has been performed on the CFK model by varying randomly all the parameters in the equation. In general, these investigations indicate that the averages of the model predictions often are relatively insensitive to changes in many physiological measurements over the normal range of the population, varying by 0.1% COHb.

If we assume that the error present in the CFK model prediction of COHb is negligible compared with the error present in the observed variable, BCO, then the observed BCO readings should be plotted on the vertical axis and the BCO estimates predicted by the CFK should be plotted on the horizontal axis (Figure 4). The result of reversing the axes and carrying out standard regression on the 615 nonsmokers in the sample is a straight line with slope 1.00 and R-squared = 0.566, suggesting that the linear model explains about 57% of the variability. The line does not, however, pass through the origin; rather it is offset by the amount 1.8 ppm breath CO, or about 0.36% COHb. Again, the model tends to underestimate the actual breath levels of respondents in the Washington, DC, area, but it does so in a consistent fashion.

Orthogonal Regression Model Predicted COHb vs. Observed Breath COHb. We can assume that there is error in both the predicted BCO and observed BCO variables because we are not measuring COHb, but are using the model predictions and breath CO measurements as surrogates for the subjects' COHb. Since there are errors in both these COHb estimates multiplication of % COHb by 5 ppm CO/%COHb to obtain BCO does not change the error relation. To handle this situation, we can apply orthogonal regression (principal component analysis). This technique finds the unique straight line which minimizes the sum of squares of the perpendicular distance from the line to any point. That is, orthogonal regression minimizes the linear model prediction error with respect to both variables simultaneously.

The resulting orthogonal regression line, when applied to the 615 nonsmokers in Washington, DC, passes almost exactly through the origin with an intercept of -0.4 ppm (Figure 5), and has a slope of 0.685.

WASHINGTON DC BREATH CO STUDY

OBSERVED VS PREDICTED(SHAPE)

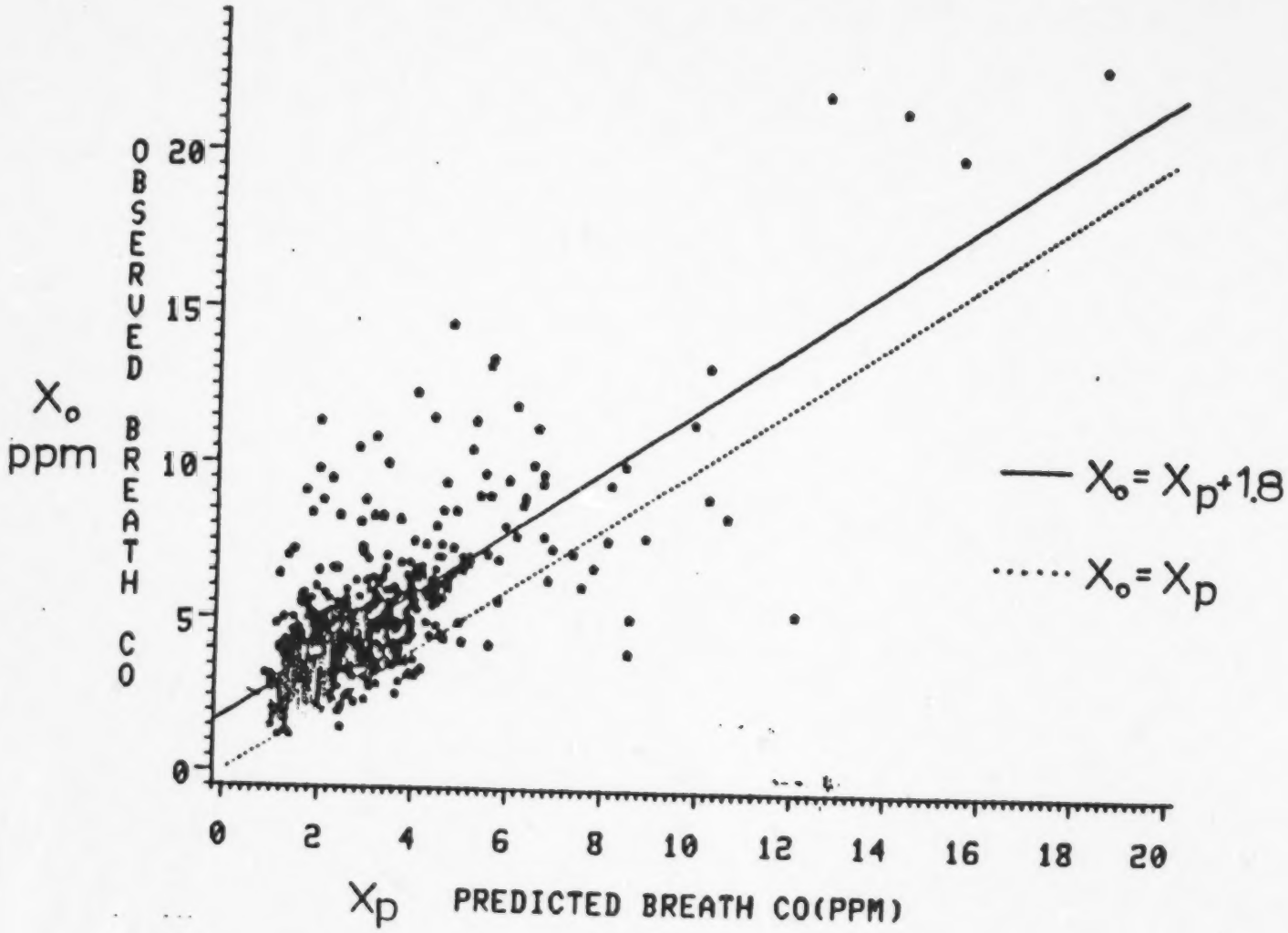

FIGURE 4. AXES REVERSED. OBSERVED BREATH CO CONCENTRATION (X_o) VERSUS PREDICTED BREATH CO CONCENTRATION (X_p) IN WASHINGTON, D.C.: EXCLUDING 10 OUTLIERS N-615 PERSON-DAYS.

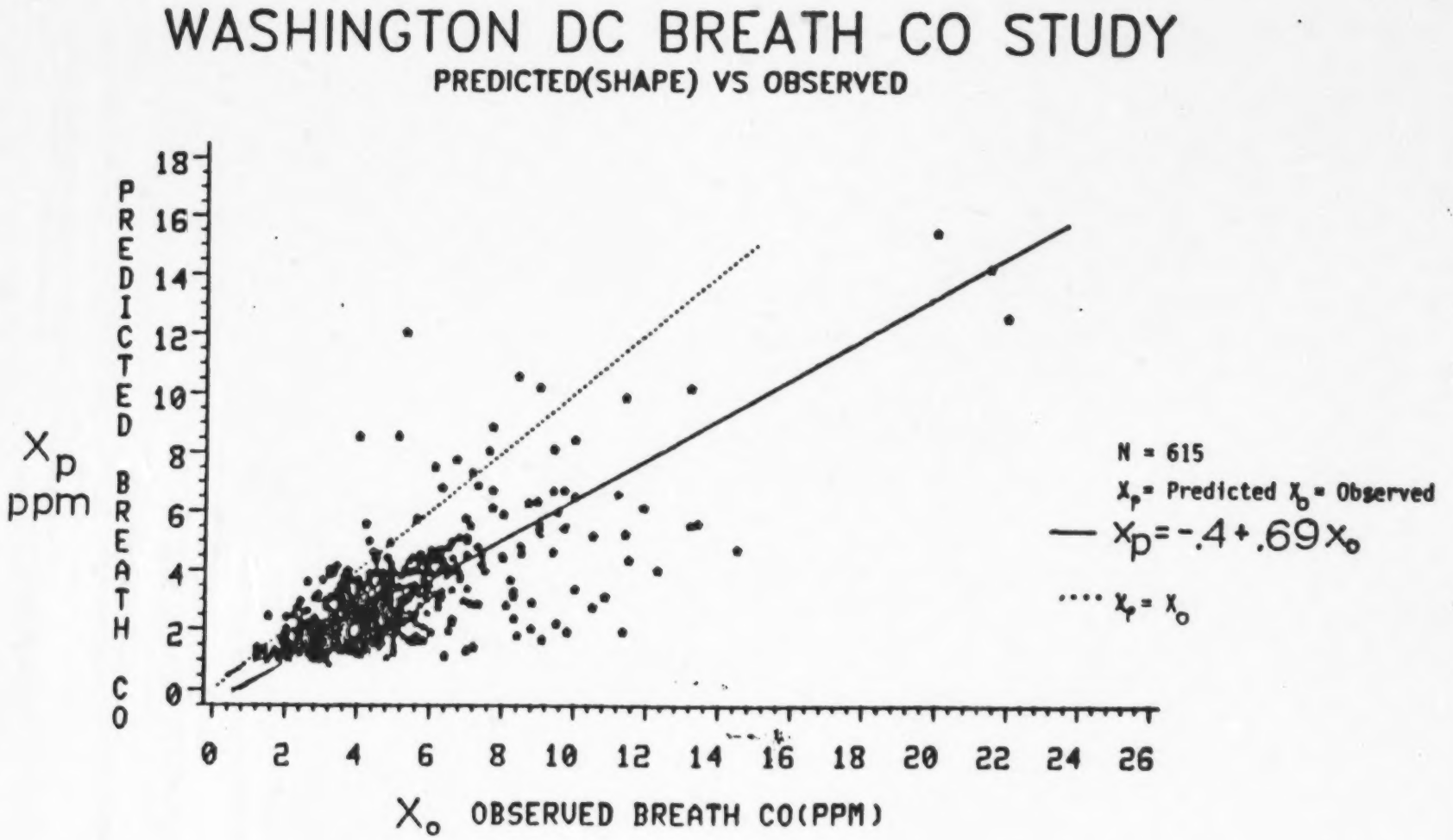

FIGURE 5. ORTHOGONAL REGRESSION: PREDICTED BREATH CO (X_p) CONCENTRATION VERSUS OBSERVED BREATH CO CONCENTRATION (X_o) IN WASHINGTON, D.C.: EXCLUDING 10 OUTLIERS N=615 PERSON-DAYS.

Discussion

A summary of the comparisons between observed breath CO and predicted breath CO is shown in Table I.

TABLE 1

Predicted vs. Observed Breath CO Concentrations

	Washington, DC		
Observed Breath CO (Nearest ppm)	N	Predicted Breath CO (Mean)	Ratio (Pred/ Obs)
2	58	1.6	0.80
3	155	1.9	0.63
4	165	2.4	0.60
5	123	2.9	0.58
6	58	3.6	0.60
7	31	4.2	0.60
8	14	5.1	0.64
9	13	5.3	0.59
10	8	5.0	0.50

The discrepancy between the breath CO estimation of COHb and the CO exposure model estimation of COHb that is shown for Washington, DC, was also found for the Denver, Colorado, data. In both cities, the average breath CO exceeded the predicted breath CO by 1.7 ppm in Denver, and by 1.8 ppm in Washington. Because the comparison results are similar, the Denver data[3] will not be discussed here.

There are several possible explanations for the observed discrepancies which are being investigated at this time. These possible sources of uncertainty are discussed in detail below.

1. The CO end-tidal breath measurement estimates of COHb may be overestimates of COHb.

The quality assurance of the breath CO measurements were discussed previously. Smith[12] and Wallace[13] have pointed out that the CO concentration in respired air has an effect on the measured breath CO, even though one follows the standard procedure of holding one's breath for 20 seconds and collecting only the final fraction for analysis. Wallace's equation, based on 130 measurements on himself, is

$$\text{measured breath CO} = .83 \text{ alveolar CO} + .17 \text{ inspired air CO}.$$

Thus, if room air is "clean" (inspired air CO < alveolar CO), the measured breath CO will underestimate the true alveolar CO, and vice versa. Only if the room air is at the same concentration as alveolar CO will the measured breath CO equal the true alveolar concentration.

An experiment was done to determine the variation among people in the strength of the this effect. Four persons were tested at three different CO levels (10, 30, 50 ppm) by breathing from a spirometer, as well as breathing in the room air. (The testing was repeated in reverse order to eliminate physiological changes or carry-over in the lungs.) The measured slopes for these inhaled CO values were 0.16, 0.22, 0.24, and 0.39, indicating that the effect of the inspired air on measured breath levels is common to most persons, and is of the order of 20%. If the 4 subjects measured had 2% COHb which would equilibrate at 10 ppm alveolar CO and they inspired 0 ppm CO, their BCO values would be 8.4, 7.8, 7.6, and 6.1 ppm CO.

However, when Jones, et al.,[5] and Stewart, et al.,[6] developed their calibration curves to relate BCO to measured COHb, the ambient CO inhaled was not measured so no correction for BCO is possible for their results. If our subjects inspired a different CO concentration than the average inspired CO of the original COHb-BCO experiment, then there could be a difference in the calculated COHb values.

Uncertainty in the measurements of blood COHb during the calibration below 2% COHb may be important since preparation of a 0% COHb standard is quite difficult. Finally, the original calibrations of BCO vs. COHb measured CO by different techniques than our PEM CO, so a minor breath component interference in one method might not appear in the other method, thereby leading to a difference beetween them.

2. The PEM CO data may be underestimates of CO exposures:

The measurement of exposures with the portable COED I monitors (PEM) had the following major differences from the breath measurements: exposure measurements were made with many different battery-powered instruments under varying temperature conditions, instead of a single stationary instrument operating off line power in a central laboratory with nearly constant conditions.

Personal exposures to CO were measured with a portable battery-powered instrument (the COED I) consisting of a modified GE CO-3 detector and a MAGUS DL-1 data logger.[2] Outdoor concentrations were measured at 15 locations in Denver and 11 in Washington, DC using EPA-approved instruments employing non-dispersive infrared (NDIR) methods. Daily calibrations were performed on the COED and NDIR instruments. Periodic audits were performed during the course of the study by technicians from EMSL-RTP.

Quality control audits of the PEMs and NDIR instruments showed the following results:

- Side-by-side readings at fixed stations in Denver and Washington resulted in average underestimates of about 15% compared to the reference methods.
- A substantial number of COED readings were 0.0 ppm when the collocated reference monitor was reading between 0.1 and 1.4 ppm, indicating a non-linear "threshold" at different levels for different monitors.
- Audits of the COEDs at different span gas concentrations showed an increased tendency to read low at the lowest (5.5 ppm) span gas concentrations.

- Each PEM was calibrated with 0.0 ppm and 40 ppm (50 ppm at Washington, DC) before and after monitoring in the field. The PEM observed readings were corrected with an average intercept and average slope from the pre- and post- calibrations. Some of the nonlinearity detected at 0.0 ppm may have been due to the inability of PEM's to record negative values (they are recorded as the absolute values). The correction of PEM readings by an average intercept which was always positive may have caused an artificial reduction in the early phase of the exposure measurements. Later measurements were performed by zeroing the PEM at 1 ppm to minimize this effect.

- Audits of PEM's after monitoring in the field showed consistent decline in the readings as the battery approached the end of its charge. Denver pre- and post- calibration data were merged with a composite results file for analysis of the above phenomena. To date, no consistent factor has been found to quantify the under-reading, if any, by the PEM's. A study is underway at EMSL-RTP to explain the behavior of PEM's after 24 hours of monitoring and determine the battery effect on the calibration.

- The PEM's may be sensitive to temperature. The PEM's were calibrated at the same approximate room temperature, before and after, in the central laboratory. However, when they were brought to the subjects and the subjects placed them in use both indoors and outdoors, they may have been operated at lower temperatures. Although the PEM is temperature compensated, the combined CO detector - data logger system may have been affected by low temperature operation and thermal transients.

3. Model or model elements may lead to underestimates of COHb:

Many physiological measurements that are difficult to evaluate enter the Coburn equation.[11,14] The Haldane constant M, endogenous CO production rate V_{CO}, capillary oxygen pressure P_{cO2}, and other variables all have a considerable range of possible values. Our choices of these parameters (M=245, V_{CO}=.0105 ml/min) lead to a typical endogenous COHb of 0.25% and a ratio of about 0.2% COHb per ppm breath CO. These values agree well with previously reported values.[5-10] An increase in the endogenous CO production rate would improve the fit, but the size of the increment required for optimum agreement appears large.

The first possible source of the discrepancy, an uncertainty in the BCO-COHb relationship, was evaluated by comparisons to the measurements of COHb reported in the NHANES II study. The National Health and Nutrition Examination Survey (NHANES II), carried out in 64 locations between 1976 and 1980,[15] is the most complete and trustworthy study of carboxyhemoglobin levels in the U.S. population. Acceptable COHb determinations were obtained for a nationwide sample of 8,409 persons ages 3-74 years.[15] Analysis was by spectrophotometry, with extensive quality assurance including 200 determinations by gas chromatography at a separate laboratory. These data for residents of large central cities agree extremely closely with the observed distributions of breath CO concentrations in Denver, assuming the standard relationship of 5 ppm breath CO per 1% COHb. The percentage of nonsmokers exceeding 2% COHb (10 ppm CO) in winter was 8.5% nationwide compared to our estimate of 10.2% in Denver, and 5.1% in Washington. The mean COHb level

for nonsmokers in large center cities in winter was 1.27%, compared to our estimates of 1.40% for Denver and 1.02% for Washington. This suggests that the breath CO data base is not out of line in relation to previous U.S. data.

The second potential source of underestimation, the PEM measurement, is being evaluated by a controlled laboratory study of the PEM under field operating conditions. The report should be available shortly.

The third potential source of underestimation, the Coburn COHb-CO uptake model,[11] is currently being evaluated in the EPA Clinical Study Laboratory. Preliminary results using physiological measured values as input variables for the CFK equation show an average 8% underprediction of the COHb measured using an IL-282 CO-oximeter.[14] The addition of breath CO analyses to the protocol and the addition of an independent COHb analysis by gas chromatography in order to better establish the absolute value of the measured COHb would provide additional useful information for our study.

CONCLUSIONS

The procedures for sampling and analyzing exhaled breath for carbon monoxide were shown to be simple, precise, and widely accepted by the general public.[3,4] We consider that this approach has been demonstrated and it is available for future studies of this type by Federal, State, and local agencies where breath analyses are appropriate.

The breath CO levels for Denver and Washington agreed well with NHANES II COHb measurements for cities of similar size. However, in both cities, breath CO levels were higher than could be accounted for by measured exposures, possibly due to the observed decreases in sensitivity of the monitoring instrument toward the end of the monitoring period.

The relationship shown by the orthogonal regression is probably the best representation of the comparison of these two estimates of COHb. The discrepancy between them is believed to be an effect of all three possible sources of the difference acting together since preliminary analysis indicates that no single source is of a magnitude that could explain the differences by itself.

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ASSUMPTIONS USED IN CFK MODEL TO COMPUTE BLOOD COHb LEVELS FROM CO EXPOSURES IN DENVER-WASHINGTON, DC, FIELD STUDIED

- Haldane Constant M = 245
- Endogenous CO Production Rate V_{CO} = 0.0105 ml/min.
- Altitude 0 ft. Washington, DC and 5280 ft. Denver
- Barometric Pressure P_B = 760 mm Washington, DC and Observed Denver
- Age and Sex of each participant used in SHAPE
- Height H = 69 inches (median) assumed for Males
  64 inches (median) assumed for Females
- Hb = 15.16 gms (median) assumed for Males
  13.43 gms (median) assumed for Females
- Weight (W) calculated based on sex, age, and height with equations (HANES I Survey)
- The blood volume (Marcus, 1980a)

  B_V = -4670 + 46.6 x 2.54 H(in) + 21.6 W(lb)/2.2(ml)
- The capillary O_2 pressure (Lambertson, et al., 1952)

  $P_{C_{O_2}}$ = 100 - 137.4 (.0000386 Alt.) (mmHg)
- Basal diffusion rate (Mohsenifar, et al., 1982)

  D_{LB} = -61 - .075 Age + 1.131 H + .975 Hb (ml/min/mmHg)
- For each activity code a reasonable activity level was assumed which in turn was converted to 5 possible levels of metabolic rate (.7, 1.0, 1.3, 2.6, & 4)
- The alveolar ventilation rate (David Mage, 1983)

  V_A = 7.5 (1 + [metabolic rate - .8]) x 1000 (ml/min)
- The lung diffusion rate (David Mage, 1983)